REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Entry of this amendment is respectfully requested. The amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disc containing the above named sequence, SEQUENCE ID NUMBERS 1-22 in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "Patent-In" provided by the PTO. The information contained in the computer readable disc is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

The Commissioner is authorized to charge any fees, including extension fees, which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-68110-1/DJB/JJD).

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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Dated: April 24, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning at page 6, line 21, has been amended as follows:

– Figure 2 (SEQ ID NO:1) shows an embodiment of a nucleic acid (mRNA) which includes a sequence encoding an angiogenesis protein, AAA4. The start and stop codons are underlined. –

Paragraph beginning at page 6, line 23, has been amended as follows:

– Figure 3 (SEQ ID NO:2) shows the open reading frame of a nucleic acid sequence encoding AAA4. The start and stop codons are underlined. –

Paragraph beginning at page 6, line 25, has been amended as follows:

– Figure 4 (SEQ ID NO:3) shows an embodiment of the amino acid sequence of AAA4. The signal peptide is double underlined, and the transmembrane sequence is underlined. In one embodiment herein, AAA4 is soluble. Thus, the signal peptide can be omitted, and the transmembrane domain deleted, inactivated, or truncated. –

Paragraph beginning at page 7, line 1, has been amended as follows:

– Figure 5 shows peptides AAA4p1 (SEQ ID NO:4) and AAA4p2 (SEQ ID NO:5). –

Paragraph beginning at page 7, line 4, has been amended as follows:

– Figure 7 (SEQ ID NO:6) shows an embodiment of a nucleic acid sequence encoding an angiogenesis protein, AAA1. A putative stop codon is underlined. –

Paragraph beginning at page 7, line 6, has been amended as follows:

– Figure 8 (SEQ ID NO:7) shows an embodiment of an amino acid sequence for AAA1. A transmembrane domain is underlined. In one embodiment, AAA1 is soluble. In preferred

embodiments, the transmembrane domain is deleted or inactivated, or AAA1 is truncated to delete the transmembrane domain. –

Paragraph beginning at page 7, line 10, has been amended as follows:

– Figure 9 shows AAA1p1 (SEQ ID NO:8) and AAA1p2 (SEQ ID NO:9). –

Paragraph beginning at page 7, line 13, has been amended as follows:

– Figure 11 (SEQ ID NO:10) shows an embodiment of a nucleic acid, mRNA, which comprises a sequence encoding an angiogenesis protein, Edg-1. The start and stop codons are underlined. –

Paragraph beginning at page 7, line 15, has been amended as follows:

– Figure 12 (SEQ ID NO:11) shows the open reading frame encoding Edg-1, wherein the start and stop codons are underlined. –

Paragraph beginning at page 7, line 18, has been amended as follows:

– Figure 13 (SEQ ID NO:12) shows an embodiment of an amino acid sequence for an angiogenesis protein, Edg-1, wherein the transmembrane domains are underlined. In a preferred embodiment herein, a soluble form of Edg-1 is provided. In one embodiment, the transmembrane domains are deleted, inactivated, and/or the protein is truncated so as to exclude the domains (with or without re-ligation of remaining soluble regions). –

Paragraph beginning at page 7, line 23, has been amended as follows:

– Figure 14 (SEQ ID NOS:13-16) depicts four peptide sequences provided herein and their respective solubilities. –

Paragraph beginning at page 8, line 3, has been amended as follows:

– Figure 17 (SEQ ID NO:17) shows an embodiment of a nucleic acid sequence which includes the coding sequence for a tissue remodeling protein, alpha 5 beta 1 integrin (sometimes referred to as VLA-5), wherein the start and stop codon are underlined. –

Paragraph beginning at page 8, line 6, has been amended as follows:

– Figure 18 (SEQ ID NO:18) shows an embodiment of an amino acid sequence of a tissue remodeling protein, alpha 5 beta 1 integrin, wherein a transmembrane domain is underlined. –

Paragraph beginning at page 8, line 15, has been amended as follows:

– Figure 21 (SEQ ID NO:19) shows an embodiment of a nucleic acid sequence which includes the coding sequence for an angiogenesis protein, endomucin, wherein the start and stop codon are boxed. –

Paragraph beginning at page 8, line 17, has been amended as follows:

– Figure 22 (SEQ ID NO:20) shows an embodiment of an amino acid sequence of an angiogenesis protein, endomucin, wherein a signal sequence is bolded and a transmembrane domain is underlined. –

Paragraph beginning at page 8, line 19, has been amended as follows:

– Figure 23 (SEQ ID NO:21) shows an embodiment of a nucleic acid sequence which includes the coding sequence for an angiogenesis protein, matrix metalloproteinase 10 (also called stromolysin 2), wherein the start and stop codon are boxed. –

Paragraph beginning at page 16, line 20, has been amended as follows:

– The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. For example, cytokine receptors are characterized by a cluster of cysteines and a WSXWS (W= tryptophan, S= serine, X=any amino acid) motif (SEQ ID NO:22). Immunoglobulin-like domains are highly conserved. Mucin-like domains may be involved in cell adhesion and leucine-rich repeats participate in protein-protein interactions. –

Paragraph beginning at page 32, line 16, has been amended as follows:

– In a preferred embodiment, when the angiogenesis protein is to be used to generate antibodies, for example for immunotherapy, the angiogenesis protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller angiogenesis protein will be able to bind to the full length protein. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity. In a preferred embodiment, the epitope is selected from AAA4p1 (SEQ ID NO:4) and AAA4p2 (SEQ ID NO:5). In another preferred embodiment the epitope is selected from AAA1p1 (SEQ ID NO:8) and AAA1p2 (SEQ ID NO:9). In another preferred embodiment the epitope is selected from AAA7p1 (SEQ ID NO:13), AAA7p2 (SEQ ID NO:14), AAA7p3 (SEQ ID NO:15) and AAA7p1m (SEQ ID NO:16). –

Paragraph beginning at page 47, line 17, has been amended as follows:

– In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "angiogenesis proteins". In preferred embodiments the angiogenesis protein is as depicted in Figures 4, 8, 13, 18, and 22 (SEQ ID NOS:3, 7, 12, 18, and 20) or encoded by the sequences shown in figures 2, 3, 7, 12, 17, 21 and 23 (SEQ ID NOS:1, 2, 6, 11 17, 19, and 21). The angiogenesis protein may be a fragment, or alternatively, be the full length protein to a fragment shown herein. –

Please replace the paragraph beginning at page 47, line 27, with the following rewritten paragraph:

– In a preferred embodiment, the fragment is from AAA1. Preferably, the fragment includes a non-transmembrane region. In a preferred embodiment, the AAA1 fragment has an N-terminal Cys to aid in solubility. Preferably, the fragment is selected from AAA1p1 (SEQ ID NO:8) and AAA1p2 (SEQ ID NO:9). –

Paragraph beginning at page 48, line 1, has been amended as follows:

– In a preferred embodiment, the fragment is charged and from the c-terminus of AAA4. In one embodiment, the c-terminus of the fragment is kept as a free acid and the n-terminus is a free amine to aid in coupling, i.e., to cysteine. In one embodiment the fragment is an internal peptide overlapping hydrophilic stretch of AAA4. In a preferred embodiment, the termini is blocked. Preferably, the fragment of AAA4 is selected from AAA4p1 (SEQ ID NO:4) or AAA4p2 (SEQ ID NO:5). In another preferred embodiment, the fragment is a novel fragment from the N-terminal. In one embodiment, the fragment excludes sequence outside of the N-terminal, in another embodiment, the fragment includes at least a portion of the N-terminal. "N-terminal" is used interchangeably herein with "N-terminus" which is further described above. –

On page 183, immediately preceding the claims, the enclosed Sequence Listing was inserted into the text.